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DATE: Thursday, June 03, 2004

Hide?	Set Name	Query	Hit Count
		DB=PGPB,USPT,USOC,EPAB,JPAB,DWPI; PLUR=YES; OP=ADJ	
☐	L1	Rothberg-B$.in. or Sawada-R$.in. or Barton-J$.in.	1189
☐	L2	histocompatibility iron loading or HFE	4274
☐	L3	(polymorphi$ or mutat$ or variant)same (exon 2)	853
☐	L4	L3 and l2	11
☐	L5	L4 and exon 4	9
☐	L6	hybridiz$ same microchip	603
☐	L7	L6 and l4	4
☐	L8	l1 and l2	5
☐	L9	6025130.pn. or 6140305 or 6509442.pn.	11
☐	L10	l2 and 435/6	96
☐	L11	L10 and l3	9

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NEWS 2		"Ask CAS" for self-help around the clock
NEWS 3	JAN 27	Source of Registration (SR) information in REGISTRY updated and searchable
NEWS 4	JAN 27	A new search aid, the Company Name Thesaurus, available in CA/CAplus
NEWS 5	FEB 05	German (DE) application and patent publication number format changes
NEWS 6	MAR 03	MEDLINE and LMEDLINE reloaded
NEWS 7	MAR 03	MEDLINE file segment of TOXCENTER reloaded
NEWS 8	MAR 03	FRANCEPAT now available on STN
NEWS 9	MAR 29	Pharmaceutical Substances (PS) now available on STN
NEWS 10	MAR 29	WPIFV now available on STN
NEWS 11	MAR 29	New monthly current-awareness alert (SDI) frequency in RAPRA
NEWS 12	APR 26	PROMT: New display field available
NEWS 13	APR 26	IFIPAT/IFIUDB/IFICDB: New super search and display field available
NEWS 14	APR 26	LITALERT now available on STN
NEWS 15	APR 27	NLDB: New search and display fields available
NEWS 16	May 10	PROUSDDR now available on STN
NEWS 17	May 19	PROUSDDR: One FREE connect hour, per account, in both May and June 2004
NEWS 18	May 12	EXTEND option available in structure searching
NEWS 19	May 12	Polymer links for the POLYLINK command completed in REGISTRY
NEWS 20	May 17	FRFULL now available on STN
NEWS 21	May 27	STN User Update to be held June 7 and June 8 at the SLA 2004 Conference
NEWS 22	May 27	New UPM (Update Code Maximum) field for more efficient patent SDIs in CAplus
NEWS 23	May 27	CAplus super roles and document types searchable in REGISTRY
NEWS 24	May 27	Explore APOLLIT with free connect time in June 2004

NEWS EXPRESS	MARCH 31 CURRENT WINDOWS VERSION IS V7.00A, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 26 APRIL 2004
NEWS HOURS	STN Operating Hours Plus Help Desk Availability
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FILE 'HOME' ENTERED AT 11:26:33 ON 03 JUN 2004

=> file .biotech caplus
COST IN U.S. DOLLARS                                    SINCE FILE      TOTAL
                                                           ENTRY    SESSION
FULL ESTIMATED COST                                         0.21       0.21

FILES 'MEDLINE, BIOTECHDS, EMBASE, BIOSIS, SCISEARCH, CANCERLIT, CAPLUS'
ENTERED AT 11:26:42 ON 03 JUN 2004
ALL COPYRIGHTS AND RESTRICTIONS APPLY.  SEE HELP USAGETERMS FOR DETAILS.

7 FILES IN THE FILE LIST

=> s rothberg B?/au or sawada R?/au or barton J?/au
L1         6088 ROTHBERG B?/AU OR SAWADA R?/AU OR BARTON J?/AU

=> s histocompatibility iron load### or HFE
L2         6857 HISTOCOMPATIBILITY IRON LOAD### OR HFE

=> s (polymorphi? or mutation or mutant or variant) and (l1 or L2)
L3         4246 (POLYMORPHI? OR MUTATION OR MUTANT OR VARIANT) AND (L1 OR L2)

=> s l3 and (exon 20
UNMATCHED LEFT PARENTHESIS 'AND (EXON'
The number of right parentheses in a query must be equal to the
number of left parentheses.

=> s l3 and (exon 2)
L4           41 L3 AND (EXON 2)

=> dup rem l4 1-4
'1-4' IS NOT VALID.  VALID FILE NAMES ARE 'MEDLINE, BIOTECHDS, EMBASE, BIOSIS,
SCISEARCH, CANCERLIT, CAPLUS'
You have entered a file name of duplicates to keep that is not
referenced by any of the L#s specified for this DUPLICATE command.
The file names of duplicates that can be kept are listed above.
Please enter one of these file names.

=> dup rem l4
PROCESSING COMPLETED FOR L4
L5            17 DUP REM L4 (24 DUPLICATES REMOVED)

=> s l5 and (exon 4)
L6             6 L5 AND (EXON 4)

=> s l17 and (hybridiz and (microchip or array))
AND IS NOT A RECOGNIZED COMMAND
The previous command name entered was not recognized by the system.
For a list of commands available to you in the current file, enter
"HELP COMMANDS" at an arrow prompt (=>).

=> s  (hybridiz and (microchip or array))
L7             1 (HYBRIDIZ AND (MICROCHIP OR ARRAY))

=> s  (hybridiz? and (microchip or array))
L8         15485 (HYBRIDIZ? AND (MICROCHIP OR ARRAY))

=> s l5 and l8
L9             0 L5 AND L8
```

```
=> d his

     (FILE 'HOME' ENTERED AT 11:26:33 ON 03 JUN 2004)

     FILE 'MEDLINE, BIOTECHDS, EMBASE, BIOSIS, SCISEARCH, CANCERLIT, CAPLUS'
     ENTERED AT 11:26:42 ON 03 JUN 2004
L1          6088 S ROTHBERG B?/AU OR SAWADA R?/AU OR BARTON J?/AU
L2          6857 S HISTOCOMPATIBILITY IRON LOAD### OR HFE
L3          4246 S (POLYMORPHI? OR MUTATION OR MUTANT OR VARIANT) AND (L1 OR L2
L4            41 S L3 AND (EXON 2)
L5            17 DUP REM L4 (24 DUPLICATES REMOVED)
L6             6 S L5 AND (EXON 4)
L7             1 S  (HYBRIDIZ AND (MICROCHIP OR ARRAY))
L8         15485 S  (HYBRIDIZ? AND (MICROCHIP OR ARRAY))
L9             0 S L5 AND L8

=> d l8 and l4
L4 IS NOT VALID HERE
For an explanation, enter "HELP DISPLAY".

=> s l8 and l4
L10            0 L8 AND L4

=> s l8 and l3
L11           16 L8 AND L3

=> dup rem l11
PROCESSING COMPLETED FOR L11
L12            7 DUP REM L11 (9 DUPLICATES REMOVED)

=> d his

     (FILE 'HOME' ENTERED AT 11:26:33 ON 03 JUN 2004)

     FILE 'MEDLINE, BIOTECHDS, EMBASE, BIOSIS, SCISEARCH, CANCERLIT, CAPLUS'
     ENTERED AT 11:26:42 ON 03 JUN 2004
L1          6088 S ROTHBERG B?/AU OR SAWADA R?/AU OR BARTON J?/AU
L2          6857 S HISTOCOMPATIBILITY IRON LOAD### OR HFE
L3          4246 S (POLYMORPHI? OR MUTATION OR MUTANT OR VARIANT) AND (L1 OR L2
L4            41 S L3 AND (EXON 2)
L5            17 DUP REM L4 (24 DUPLICATES REMOVED)
L6             6 S L5 AND (EXON 4)
L7             1 S  (HYBRIDIZ AND (MICROCHIP OR ARRAY))
L8         15485 S  (HYBRIDIZ? AND (MICROCHIP OR ARRAY))
L9             0 S L5 AND L8
L10            0 S L8 AND L4
L11           16 S L8 AND L3
L12            7 DUP REM L11 (9 DUPLICATES REMOVED)

=> d ibib abs l6 1-6

L6   ANSWER 1 OF 6     MEDLINE on STN
ACCESSION NUMBER:   2003553775     MEDLINE
DOCUMENT NUMBER:    PubMed ID: 14633868
TITLE:              Identification of new mutations of the HFE,
                    hepcidin, and transferrin receptor 2 genes by denaturing
                    HPLC analysis of individuals with biochemical indications
                    of iron overload.
AUTHOR:             Biasiotto Giorgio; Belloli Silvana; Ruggeri Giuseppina;
                    Zanella Isabella; Gerardi Gianmario; Corrado Marcella;
                    Gobbi Elena; Albertini Alberto; Arosio Paolo
CORPORATE SOURCE:   Dipartimento Materno Infantile e Tecnologie Biomediche,
                    University of Brescia, viale Europa 11, 25123 Brescia,
                    Italy.
```

SOURCE: Clinical chemistry, (2003 Dec) 49 (12) 1981-8.
Journal code: 9421549. ISSN: 0009-9147.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200312
ENTRY DATE: Entered STN: 20031125
Last Updated on STN: 20031220
Entered Medline: 20031219

AB BACKGROUND: Hereditary hemochromatosis is a recessive disorder characterized by iron accumulation in parenchymal cells, followed by organ damage and failure. The disorder is mainly attributable to the C282Y and H63D mutations in the **HFE** gene, but additional mutations in the **HFE**, transferrin receptor 2 (TfR2), and hepcidin genes have been reported. The copresence of mutations in different genes may explain the phenotypic heterogeneity of the disorder and its variable penetrance. METHODS: We used denaturing HPLC (DHPLC) for rapid DNA scanning of the **HFE** (exons 2, 3, and 4), hepcidin, and TfR2 (exons 2, 4 and 6) genes in a cohort of 657 individuals with altered indicators of iron status. RESULTS: DHPLC identification of C282Y and H63D **HFE** alleles was in perfect agreement with the restriction endonuclease assay. Fourteen DNA samples were heterozygous for the **HFE** S65C **mutation**. In addition, we found novel mutations: two in **HFE** (R66C in **exon 2** and R224G in **exon 4**), one in the hepcidin gene (G71D), and one in TfR2 (V22I), plus several intronic or silent substitutions. Six of the seven individuals with hepcidin or TfR2 coding mutations carried also **HFE** C282Y or S65C mutations. CONCLUSION: DHPLC is an efficient method for mutational screening for the genes involved in hereditary hemochromatosis and for the study of their copresence.

L6 ANSWER 2 OF 6 MEDLINE on STN
ACCESSION NUMBER: 2001681172 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11700156
TITLE: Association of mutations in the hemochromatosis gene with shorter life expectancy.
COMMENT: Comment in: Arch Intern Med. 2002 May 27;162(10):1196-7.
PubMed ID: 12020197
AUTHOR: Bathum L; Christiansen L; Nybo H; Ranberg K A; Gaist D; Jeune B; Petersen N E; Vaupel J; Christensen K
CORPORATE SOURCE: Department of Clinical Biochemistry, Odense University Hospital, Sdr. Blvd 29, DK-5000 Odense C, Denmark.. Lise.Bathum@ouh.fyns-amt.dk
CONTRACT NUMBER: NIA-PO1-AG08761 (NIA)
SOURCE: Archives of internal medicine, (2001 Nov 12) 161 (20) 2441-4.
Journal code: 0372440. ISSN: 0003-9926.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200112
ENTRY DATE: Entered STN: 20011203
Last Updated on STN: 20020911
Entered Medline: 20011207

AB BACKGROUND: To investigate whether the frequency of carriers of mutations in the **HFE** gene associated with hereditary hemochromatosis diminishes with age as an indication that **HFE** mutations are associated with increased mortality. It is of value in the debate concerning screening for hereditary hemochromatosis to determine the significance of heterozygosity. METHODS: Genotyping for mutations in exons 2 and 4 of the **HFE** gene using denaturing gradient gel electrophoresis in 1784 participants aged 45 to 100 years from 4

population-based studies: all 183 centenarians from the Danish Centenarian Study, 601 people aged 92 to 93 years from the Danish 1905 Cohort, 400 aged 70 to 94 years from the Longitudinal Study of Aging Danish Twins, and 600 aged 45 to 67 years from a study of middle-aged Danish twins. RESULTS: All participants (N=1784) were screened for mutations in **exon 4**, and a trend toward fewer heterozygotes for the C282Y **mutation**-the **mutation** most often associated with hereditary hemochromatosis-was found. This was significant for the whole population (P=.005) and for women (P=.004) but not for men (P=.26). A group of 599 participants was screened for mutations in **exon 2**, and there was no variation in the distribution of mutations in **exon 2** in the different age groups. CONCLUSIONS: In a high-carrier frequency population like Denmark, mutations in **HFE** show an age-related reduction in the frequency of heterozygotes for C282Y, which suggests that carrier status is associated with shorter life expectancy.

L6 ANSWER 3 OF 6 MEDLINE on STN
ACCESSION NUMBER: 2001266158 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11358389
TITLE: **Mutation** analysis of the transferrin receptor-2 gene in patients with iron overload.
COMMENT: Comment in: Blood Cells Mol Dis. 2001 Jan-Feb;27(1):294-5. PubMed ID: 11358391
AUTHOR: Lee P L; Halloran C; West C; Beutler E
CORPORATE SOURCE: Department of Molecular and Experimental Medicine, Scripps Research Institute, 10550 North Torrey Pines Road, La Jolla, California 92037, USA.. plee@scripps.edu
SOURCE: Blood cells, molecules & diseases, (2001 Jan-Feb) 27 (1) 285-9.
Journal code: 9509932. ISSN: 1079-9796.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200110
ENTRY DATE: Entered STN: 20011008
Last Updated on STN: 20011008
Entered Medline: 20011004

AB Three mutations in the transferrin receptor-2 gene have recently been identified in four Sicilian families with iron overload who had a normal hemochromatosis gene, **HFE** (C. Camaschella, personal communication). To determine the extent to which mutations in the transferrin receptor-2 gene occur in other populations with iron overload, we have completely sequenced this gene in 17 whites, 10 Asians, and 8 African Americans with iron overload and a C282C/C282C **HFE** genotype, as well as 4 subjects without iron overload and homozygous for the **mutant HFE** C282Y genotype, 5 patients with iron overload and homozygous for the **mutant HFE** C282Y genotype, and 5 normal individuals. None of the individuals exhibited the Sicilian mutations, Y250X in exon 6, M172K in **exon 4**, and E60X in **exon 2**. One iron-overloaded individual of Asian descent exhibited a I238M **mutation** which was subsequently found to be a **polymorphism** present in the Asian population at a frequency of 0.0192. The presence of the I238M **mutation** was not associated with an increase in ferritin or transferrin saturation levels. Three silent **polymorphisms** were also identified, nt 1770 (D590D) and nt 1851 (A617A) and a **polymorphism** at nt 2255 in the 3' UTR. Thus, mutations in the transferrin receptor-2 gene were not responsible for the iron overload seen in our subjects.

L6 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2004:247034 CAPLUS

DOCUMENT NUMBER: 140:265588
TITLE: Primers for detection of single nucleotide **polymorphisms** in the **HFE** gene and their use in diagnosis and determination of risk of hemochromatosis
INVENTOR(S): Nadeau, James G.; Scott, Patricia B.; Spargo, Catherine A.; Dean, Cheryl H.; Garic-Stankovic, Ana
PATENT ASSIGNEE(S): Becton, Dickinson and Company, USA
SOURCE: Eur. Pat. Appl., 42 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1400597	A1	20040324	EP 2003-20862	20030915
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				

PRIORITY APPLN. INFO.: US 2002-247586 A 20020920

AB The present invention provides oligonucleotides and methods for amplifying, detecting and identifying **polymorphisms** associated with hemochromatosis. It has been found that the reduced efficiency of primer extension by DNA polymerases when the 3' end of a primer does not hybridize perfectly with the target can be adapted for use as a means for distinguishing or identifying the nucleotide in the target which is at the site where the diagnostic mismatch between the detector primer and the target occurs. The efficiency of detector primer extension is detected as an indication of the presence and/or identity of the sequence variation in the target. The inventive methods make use of hemochromatosis gene (**HFE**)-specific amplification primers and nucleotide mismatches at or near the 3' end of a detector primer to amplify fragments of the **HFE** gene and discriminate between **mutant** and wild-type alleles and single nucleotide **polymorphisms** which may occur in **exon 2** and **exon 4** of the (**HFE**) gene.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 5 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:900309 CAPLUS
DOCUMENT NUMBER: 134:52229
TITLE: Methods for detecting nucleic acid sequence variations using allele-specific detector primers
INVENTOR(S): Wright, David J.; Milla, Maria A.; Nadeau, James G.; Walker, G. Terrance
PATENT ASSIGNEE(S): Becton, Dickinson and Company, USA
SOURCE: Eur. Pat. Appl., 36 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1061135	A2	20001220	EP 2000-108366	20000417
EP 1061135	A3	20030625		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
US 2002025519	A1	20020228	US 1999-335218	19990617
CA 2306055	AA	20001217	CA 2000-2306055	20000419
JP 2001057892	A2	20010306	JP 2000-182884	20000619

US 2001009761 A1 20010726 US 2001-778168 20010207
US 2001039334 A1 20011108 US 2001-778175 20010207
PRIORITY APPLN. INFO.: US 1999-335218 A 19990617
AB The present invention provides methods for detecting and identifying sequence variations in a nucleic acid sequence of interest using a detector primer. It has been found that the reduced efficiency of primer extension by DNA polymerases when the 3' end of a primer does not hybridize perfectly with the target can be adapted for use as a means for distinguishing or identifying the nucleotide in the target which is at the site where the diagnostic mismatch between the detector primer and the target occurs. The detector primer hybridizes to the sequence of interest and is extended with polymerase. The efficiency of detector primer extension is detected as an indication of the presence and/or identity of the sequence variation in the target. The inventive methods make use of nucleotide mismatches at or near the 3' end of the detector primer to discriminate between the nucleotide sequence of interest and a second nucleotide sequence which may occur at that same site in the target. The methods are particularly well suited for detecting and identifying single nucleotide differences between a target sequence of interest (e.g., a **mutant** allele of a gene) and a second nucleic acid sequence (e.g., a wild type allele for the same gene). The method is illustrated by detecting mutations in gene **HFE** (the gene responsible for hemochromatosis) using strand-displacement amplification (SDA).

L6 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:900308 CAPLUS
DOCUMENT NUMBER: 134:67126
TITLE: Primers for detection of single nucleotide **polymorphisms** in the **HFE** gene and their use in diagnosis and determination of risk of hemochromatosis
INVENTOR(S): Nadeau, James G.; Scott, Patricia B.; Spargo, Catherine A.; Dean, Cheryl H.; Garic-Stankovic, Ana
PATENT ASSIGNEE(S): Becton, Dickinson and Company, USA
SOURCE: Eur. Pat. Appl., 36 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1061134	A2	20001220	EP 2000-107667	20000410
EP 1061134	A3	20030108		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
CA 2305849	AA	20001217	CA 2000-2305849	20000414
BR 2000002587	A	20010424	BR 2000-2587	20000606
JP 2001046085	A2	20010220	JP 2000-182852	20000619

PRIORITY APPLN. INFO.: US 1999-335217 A 19990617
AB The present invention provides oligonucleotides and methods for amplifying, detecting and identifying sequence variations associated with hemochromatosis. The method uses a panel of primers with base mismatches with the target sequence at the 3' end of the primer to discriminate between alleles. The efficiency of detector primer extension is detected as an indication of the presence and/or identity of the sequence variation in the target. The inventive methods make use of hemochromatosis gene (**HFE**)-specific amplification primers and nucleotide mismatches at or near the 3' end of a detector primer to amplify the **HFE** gene and discriminate between wild-type alleles and single nucleotide **polymorphisms** which may occur in **exon 2** and **exon 4** of the (**HFE**) gene.

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=> d his

     (FILE 'HOME' ENTERED AT 11:26:33 ON 03 JUN 2004)

     FILE 'MEDLINE, BIOTECHDS, EMBASE, BIOSIS, SCISEARCH, CANCERLIT, CAPLUS'
     ENTERED AT 11:26:42 ON 03 JUN 2004
L1          6088 S ROTHBERG B?/AU OR SAWADA R?/AU OR BARTON J?/AU
L2          6857 S HISTOCOMPATIBILITY IRON LOAD### OR HFE
L3          4246 S (POLYMORPHI? OR MUTATION OR MUTANT OR VARIANT) AND (L1 OR L2
L4            41 S L3 AND (EXON 2)
L5            17 DUP REM L4 (24 DUPLICATES REMOVED)
L6             6 S L5 AND (EXON 4)
L7             1 S  (HYBRIDIZ AND (MICROCHIP OR ARRAY))
L8         15485 S  (HYBRIDIZ? AND (MICROCHIP OR ARRAY))
L9             0 S L5 AND L8
L10            0 S L8 AND L4
L11           16 S L8 AND L3
L12            7 DUP REM L11 (9 DUPLICATES REMOVED)

=> d ibib abs l7

L7    ANSWER 1 OF 1  BIOTECHDS COPYRIGHT 2004 THOMSON DERWENT/ISI on STN
ACCESSION NUMBER: 2002-14843  BIOTECHDS
TITLE:            Nucleic acid comprising single nucleotide polymorphisms,
                  useful in forensics, paternity testing and diagnosis of
                  disease;
                     DNA primer and DNA probe immobilization for SNP detection
                     and DNA array construction
AUTHOR:           CARGILL M; IRELAND J S; LANDER E S
PATENT ASSIGNEE:  CARGILL M; IRELAND J S; LANDER E S
PATENT INFO:      US 2002037508 28 Mar 2002
APPLICATION INFO: US 2000-765081 19 Jan 2000
PRIORITY INFO:    US 2001-765081 18 Jan 2001
DOCUMENT TYPE:    Patent
LANGUAGE:         English
OTHER SOURCE:     WPI: 2002-315108 [35]
AN    2002-14843  BIOTECHDS
AB    DERWENT ABSTRACT:
      NOVELTY - Nucleic acid comprising single nucleotide polymorphisms (SNPs)
      associated with diseases, the encoded polypeptides (III) and primers and
      probes (II) for detecting (IV) them, are new.
           DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for the
      following: (1) a nucleic acid molecule (I) comprising a nucleic acid
      sequence selected from a group given in the specification (the nucleic
      acid sequence is at least 10 nucleotides in length and comprises a
      polymorphic site given in the specification, and the nucleotide at the
      polymorphic site is different from a nucleotide at the polymorphic site
      in a corresponding reference allele); (2) an allele-specific
      oligonucleotide (II) that hybridizes to a portion of a nucleic acid
      sequence selected from the group of nucleic acid sequences given in the
      specification (the portion is at least 10 nucleotides in length and
      comprises a polymorphic site given in the specification, and the
      nucleotide at the polymorphic site is different from a nucleotide at the
      polymorphic site in a corresponding reference allele); (3) an isolated
      gene product (III) encoded by the nucleic acid molecule (I); and (4) a
      method (IV) of analyzing a nucleic acid sample, comprising obtaining the
      nucleic acid sample from an individual and determining a base occupying
      any one of the polymorphic sites given in the specification.
           BIOTECHNOLOGY - Preferred Nucleic Acids: The nucleic acid sequence
      (I) is at least 15-20 nucleotides in length. The nucleotide at the
      polymorphic site is the variant nucleotide for the nucleic acid sequence
      given in the specification. The allele-specific oligonucleotide (II) is a
      probe (a central position of the probe aligns with the polymorphic site
```

of the portion) or a primer (the 3' end of the primer aligns with the polymorphic site of the portion). Preferred Methods: The nucleic acid sample in (IV) is obtained from a number of individuals, and a base occupying one of the polymorphic positions is determined in each of the individuals. The method further comprises testing each individual for the presence of a disease phenotype, and correlating the presence of the disease phenotype with the base. Preparation: The polymorphisms given in the specification were identified by re-sequencing of target sequences from individuals of diverse ethnic and geographic backgrounds by **hybridiz** ation to probes immobilized to microfabricated arrays. The strategy and principles for design and use of such arrays are generally described in WO9511995.

USE - The nucleic acids (I) comprising the SNPs and probes and primers (II) for detecting them may be used in assays (IV) for the diagnosis of diseases associated with SNPs (such as sickle cell anaemia, agammaglobulimenia, diabetes insipidus, Lesch-Nyhan syndrome, muscular dystrophy, Wiskott-Aldrich syndrome, Fabry's disease, familial hypercholesterolemia, polycystic kidney disease, hereditary spherocytosis, von Willebrand's disease, tuberous sclerosis, hereditary hemorrhagic telangiectasia, familial colonic polyposis, Ehlers-Danlos syndrome, osteogenesis imperfecta, and acute intermittent porphyria, symptoms of, or susceptibility to, multifactorial diseases of which a component is or may be genetic, such as autoimmune diseases, inflammation, cancer, diseases of the nervous system, and infection by pathogenic microorganisms, autoimmune diseases including rheumatoid arthritis, multiple sclerosis, diabetes (insulin-dependent and non-independent), systemic lupus erythematosus and Graves disease, cancers including cancers of the bladder, brain, breast, colon, esophagus, kidney, leukemia, liver, lung, oral cavity, ovary, pancreas, prostate, skin, stomach and uterus, longevity, appearance (e.g., baldness, obesity), strength, speed, endurance, fertility, and susceptibility or receptivity to particular drugs or therapeutic treatments), in forensics and in paternity testing.

EXAMPLE - Publicly available sequences for a given gene were assembled into Gap4 (http://www.biozentrum.unibas.ch/.about.biocomp/staden/Overview.html-). Polymerase Chain Reaction (PCR) primers covering each exon were designed using Primer 3 (http://www-genome.wi.mit.edu/cgi-bin/primer/primer3.cgi). Primers were not designed in regions where there were sequence discrepancies between reads. Genomic DNA was amplified in at least 50 individuals using 2.5 pmol each primer, 1.5 mM MgCl2, 100 muM dNTPs, 0.75 muM AmpliTaq GOLD (RTM) polymerase, and 19 ng DNA in a 15 mul reaction. Reactions were assembled using a PACKARD MultiPROBE (RTM) robotic pipetting station and then put in MJ 96-well tetrad thermocyclers (96 degreesC for 10 minutes, followed by 35 cycles of 96 degreesC for 30 seconds, 59 degreesC for 2 minutes, and 72 degreesC for 2 minutes). A subset of the PCR assays for each individual were run on 3% NuSieve (RTM) gels in 0.5xTBE to confirm that the reaction worked. Fo r a given DNA, 5 mul (about 50 ng) of each PCR or Reverse Transcription (RT)-PCR product were pooled (Final volume=150-200 mul). The products were purified using QiaQuick PCR (RTM) purification from Qiagen. The samples were eluted once in 35 mul sterile water and 4 mul 10xX One-Phor-All (RTM) buffer (Pharmacia). The pooled samples were digested with 0.2mu DNase I (RTM) (Promega) for 10 minutes at 37 degreesC and then labeled with 0.5 nmols biotin-N6-ddATP and 15mu Terminal Transferase (RTM) (GibcoBRL Life Technology) for 60 minutes at 37 degreesC. Both fragmentation and labeling reactions were terminated by incubating the pooled sample for 15 minutes at 100 degreesC. Low-density DNA chips (Affymetrix, Calif.) were hybridized following the manufacturer's instructions. Briefly, the hybridization cocktail consisted of 3M TMACl, 10 mM Tris pH 7.8, 0.01% Triton X-100, 100 mg/ml herring sperm DNA (Gibco BRL), 200 pM control biotin-labeled oligo. The processed PCR products were den atured for 7 minutes at 100 degreesC and then added to prewarmed (37 degreesC) hybridization solution. The chips were hybridized over-night at 44 degreesC. Chips were washed in 1+SSPET and 6+ SSPET followed

by staining with 2 mug/ml SARPE and 0.5 mg/ml acetylated BSA in 200 mul of 6xSSPET for 8 minutes at room temperature. Chips were scanned using a Molecular Dynamics scanner. Chip image files were analyzed using Ulysses (RTM) (Affymetrix) which used four algorithms to identify potential polymorphisms. Candidate polymorphisms were visually inspected and assigned a confidence value: high confidence candidates displayed all three genotypes, while likely candidates showed only two genotypes (homozygous for reference sequence and heterozygous for reference and variant). Some of the candidate polymorphisms were confirmed by ABI sequencing. Identified polymorphisms were compared to several databases to determine if they were novel. Results are shown in the specification.(1 pages)

=> d his

(FILE 'HOME' ENTERED AT 11:26:33 ON 03 JUN 2004)

FILE 'MEDLINE, BIOTECHDS, EMBASE, BIOSIS, SCISEARCH, CANCERLIT, CAPLUS' ENTERED AT 11:26:42 ON 03 JUN 2004

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L1          6088 S ROTHBERG B?/AU OR SAWADA R?/AU OR BARTON J?/AU
L2          6857 S HISTOCOMPATIBILITY IRON LOAD### OR HFE
L3          4246 S (POLYMORPHI? OR MUTATION OR MUTANT OR VARIANT) AND (L1 OR L2
L4            41 S L3 AND (EXON 2)
L5            17 DUP REM L4 (24 DUPLICATES REMOVED)
L6             6 S L5 AND (EXON 4)
L7             1 S  (HYBRIDIZ AND (MICROCHIP OR ARRAY))
L8         15485 S  (HYBRIDIZ? AND (MICROCHIP OR ARRAY))
L9             0 S L5 AND L8
L10            0 S L8 AND L4
L11           16 S L8 AND L3
L12            7 DUP REM L11 (9 DUPLICATES REMOVED)
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=> d ibib abs l12 1-7

L12 ANSWER 1 OF 7 BIOTECHDS COPYRIGHT 2004 THOMSON DERWENT/ISI on STN

ACCESSION NUMBER: 2002-19335 BIOTECHDS

TITLE: Detecting base-stacking perturbations in a nucleic acid sequence by measuring electron transfer between an intercalative redox-active moiety and DNA-modified electrodes is useful to detect disease-related point mutations; genetic disease diagnosis by point **mutation** detection and gene therapy

AUTHOR: **BARTON J K**; HILL M G; KELLEY S O

PATENT ASSIGNEE: BARTON J K; HILL M G; KELLEY S O

PATENT INFO: US 2002055103 9 May 2002

APPLICATION INFO: US 1997-753362 9 Apr 1997

PRIORITY INFO: US 2000-753362 29 Dec 2000

DOCUMENT TYPE: Patent

LANGUAGE: English

OTHER SOURCE: WPI: 2002-556514 [59]

AN 2002-19335 BIOTECHDS

AB DERWENT ABSTRACT:

NOVELTY - Detecting base-stacking perturbations in a target sequence, is new.

DETAILED DESCRIPTION - Detecting base-stacking perturbations in a target sequence comprising **hybridizing** two single stranded nucleic acids to form a complex, depositing the complex onto an electrode or addressable multielectrode **array**, adding an intercalative non-intercalative redox-active moiety to the complex to form a second complex, and measuring an electron transfer event between the electrode or **array** and the intercalative redox-active moiety. An INDEPENDENT CLAIM is also included for detecting point mutations electrocatalytically within the p53 gene, comprising: (a) forming a set

of nucleotide duplexes of approximately 20 bp (base pairs) corresponding to the 600bp region within exons 5-8 of the p53 gene, where the duplexes are derivatized with a thio-terminated linker comprised of 5-20 tau bonds; (b) depositing the duplexes onto an addressable gold multielectrode **array**; (c) denaturing the duplexes by immersing them in aqueous solution at elevated temperature for 1 minute and removing complementary strands to form a single stranded monolayer; (d) exposing the monolayer to a sample comprising PCR-amplified (polymerase chain reaction-) and fragmented p53 gene DNA under **hybridizing** conditions to form a complex; (e) rinsing the electrode-bound complex to remove any unhybridized material; (f) immersing the electrode-bound complex in a solution comprising 1.0 microM methylene blue and 1.0 mM ferricyanide; (g) measuring an electron transfer event as an indication of point mutations; and (h) repeating steps (c) to (g) using several sample solutions.

BIOTECHNOLOGY - Preferred Method: The base stacking perturbations are point mutations, protein-DNA adducts and/or adducts between any chemical entity and the target sequence. The intercalative redox-active moiety is either non-covalently adsorbed or cross-linked to the complex and is an intercalator selected from phenanthridines, phenothiazines, phenazines, acridines and anthraquinones, most preferably daunomycin, or is a part of a protein most preferably mut Y. A non-intercalative redox-active moiety may also be added at the same time, and this is preferably a ferrocene, ferricyanide, hexacyanoruthenate or hexacyanoosmate. Where both moieties are used the intercalator is preferably methylene blue and the non-intercalator is ferricyanide. The electrode or **array** is gold or carbon. One of the nucleic acids is derivatized with a functionalized linker, preferably one comprising 5-20 tau bonds and thiol- terminated or amine- terminated. Preferably the addressable multielectrode **array** is comprised of a monolayer of oligonucleotide duplexes of 5-10 bp deposited on the **array**, where each duplex is derivatized on one end with a functionalized linker and on the other end with a single stranded overhang of known sequence, where one of the single stranded nucleic acids contains a second single stranded overhang complementary to the overhang on the electrode or **array**.

MECHANISM OF ACTION - Gene Therapy.

USE - The invention is used to detect genetic disease-related point mutations.

EXAMPLE - The charge for daunomycin at DNA-modified electrodes containing different single-base mismatches was analyzed. The seven different mismatched duplexes were obtained by **hybridization** of the thiol-modified sequence SH-5 AGTACAGTCATCGCG with various complements each containing one mismatch. The charges were calculated by integrating background subtracted cyclic voltammograms. Melting points temperatures of the oligomers in solution were measured by monitoring duplex hypochromicity at 260 nm using samples that contained 10 microM duplex, 100 mM MgCl2 and 100 mM phosphate at pH 7.0. Colorimetric analysis confirmed that the attenuation of the characteristic response was strongly dependent on the identity of the **mutation**. In general pyrimidine-pyrimidine and purine-pyrimidine mismatches caused marked decreases in the electrochemical signals while the one GA mismatch studied did not show a measurable effect (see figure). (13 pages)

L12 ANSWER 2 OF 7 BIOTECHDS COPYRIGHT 2004 THOMSON DERWENT/ISI on STN
ACCESSION NUMBER: 2002-14880 BIOTECHDS
TITLE: Microfabricated 384-lane capillary **array** electrophoresis bioanalyzer for ultrahigh-throughput genetic analysis;
capillary **array** electrophoresis apparatus for ultra-high throughput screening, genetic variation detection, **mutation** diagnosis, functional genomics and pharmacogenomics
AUTHOR: EMRICH CA; TIAN HJ; MEDINTZ IL; MATHIES RA

CORPORATE SOURCE: Univ Calif Berkeley; Univ Calif Berkeley
LOCATION: Mathies RA, Univ Calif Berkeley, Dept Chem, Berkeley, CA 94720 USA
SOURCE: ANALYTICAL CHEMISTRY; (2002) 74, 19, 5076-5083
ISSN: 0003-2700
DOCUMENT TYPE: Journal
LANGUAGE: English
AN 2002-14880 BIOTECHDS
AB AUTHOR ABSTRACT - A microfabricated 384-lane capillary **array** electrophoresis device is developed and utilized for massively parallel genetic analysis. The 384 capillarylanes, arrayed radially about the center of a 200-mm-diameter glass substrate sandwich, are constructed using scalable microfabrication techniques derived from the semiconductor industry. Samples are loaded into reservoirs on the perimeter of the wafer, separated on the 8-cm-long poly(dimethylacrylamide) gel-filled channels, and detected with a four-color rotary confocalfluorescence scanner. The performance and throughput of this bioanalyzer are demonstrated by simultaneous genotyping 384 individuals for the common hemochromatosis-linked H63D **mutation** in the human **HFE** gene in only 325 s. This lab-on-a-chip device thoroughly exploits the power of microfabrication toproduce high-density capillary electrophoresis arrays and to use them forhigh-throughput bioanalysis. (8 pages)

L12 ANSWER 3 OF 7 MEDLINE on STN DUPLICATE 1
ACCESSION NUMBER: 2002680512 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12441151
TITLE: Plastic biochannel **hybridization** devices: a new concept for microfluidic DNA arrays.
AUTHOR: Lenigk Ralf; Liu Robin H; Athavale Mahesh; Chen Zhijian; Ganser Dale; Yang Jianing; Rauch Cory; Liu Yingjie; Chan Betty; Yu Huinan; Ray Melissa; Marrero Robert; Grodzinski Piotr
CORPORATE SOURCE: Motorola PSRL Microfluidics Laboratory, Tempe, AZ, USA.. Ralf.Lenigk@asu.edu
SOURCE: Analytical biochemistry, (2002 Dec 1) 311 (1) 40-9. Journal code: 0370535. ISSN: 0003-2697.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200306
ENTRY DATE: Entered STN: 20021121
Last Updated on STN: 20030611
Entered Medline: 20030610
AB Conventional DNA **hybridization** assay kinetics depends solely on the diffusion of target to surface-bound probes, causing long **hybridization** times. In this study, we examined the possibilities of accelerating the **hybridization** process by using microfluidic channels ("biochannels") made of polycarbonate, optionally with an integrated pump. We produced two different devices to study these effects: first, **hybridization** kinetics was investigated by using an eSensor electrochemical DNA detection platform allowing kinetic measurements in homogenous solution. We fabricated an integrated cartridge for the chip comprising the channel network and a micropump for the oscillation of the **hybridization** mixture to further overcome diffusion limitations. As a model assay, we used an assay for the detection of single-nucleotide **polymorphisms** in the **HFE** -H gene. Second, based on the biochannel approach, we constructed a plastic microfluidic chip with a network of channels for optical detection of fluorescent-labeled targets. An assay for the simultaneous detection of four pathogenic bacteria surrogate strains from multiple samples was developed for this device. We observed high initial **hybridization** velocities and a fast attainment of equilibrium for the biochannel with

integrated pump. Experimental results were compared with predictions generated by computer simulations.

L12 ANSWER 4 OF 7 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN DUPLICATE 2
ACCESSION NUMBER: 2001:544374 SCISEARCH
THE GENUINE ARTICLE: 449EJ
TITLE: Simultaneous identification of mutations by dual-parameter multiplex **hybridization** in peptide nucleic acid-containing virtual arrays
AUTHOR: Igloi G L (Reprint)
CORPORATE SOURCE: Univ Freiburg, Inst Biol 3, Schanzlestr 1, D-79104 Freiburg, Germany (Reprint); Univ Freiburg, Inst Biol 3, D-79104 Freiburg, Germany
COUNTRY OF AUTHOR: Germany
SOURCE: GENOMICS, (15 JUN 2001) Vol. 74, No. 3, pp. 402-407. Publisher: ACADEMIC PRESS INC, 525 B ST, STE 1900, SAN DIEGO, CA 92101-4495 USA. ISSN: 0888-7543.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 12
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB The physical entrapment of peptide nucleic acids (PNA) in electrophoresis media provides a system for performing real-time **hybridization**. DNA strands fully complementary to the target PNA are retarded compared to single-nucleotide mismatched strands. A second parameter, that of amplicon length, has been introduced to perform multiplex analyses on several mutations simultaneously. Size fractionation creates a virtual **array** of PCR products that can **hybridize** to one of a set of **mutation**-specific PNAs present within the matric. Each targeted **mutation** can be identified by the size of its corresponding amplicon. Its genotype is characterized by its interaction with a specific PNA that gives a visually resolved distinction between wildtype and **mutant** allele. In: contrast to conventional **hybridization**, heterozygotes are readily distinguished from homozygotes. Using a capillary electrophoresis-based DNA sequencer, this approach has been used to automate the identification of the H63D, S65C, and C282Y mutations in the hereditary hemochromatosis gene. (C) 2001 Academic Press.

L12 ANSWER 5 OF 7 MEDLINE on STN DUPLICATE 3
ACCESSION NUMBER: 2001026267 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11017050
TITLE: **Mutation** detection by electrocatalysis at DNA-modified electrodes.
COMMENT: Comment in: Nat Biotechnol. 2000 Oct;18(10):1042-3. PubMed ID: 11017039
Erratum in: Nat Biotechnol 2000 Dec;18(12):1318
AUTHOR: Boon E M; Ceres D M; Drummond T G; Hill M G; **Barton J K**
CORPORATE SOURCE: Division of Chemistry and Chemical Engineering, California Institute of Technology, Pasadena, CA 91125, USA.
CONTRACT NUMBER: GM61077 (NIGMS)
SOURCE: Nature biotechnology, (2000 Oct) 18 (10) 1096-100. Journal code: 9604648. ISSN: 1087-0156.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200011
ENTRY DATE: Entered STN: 20010322
Last Updated on STN: 20010702
Entered Medline: 20001115

AB Detection of mutations and damaged DNA bases is important for the early diagnosis of genetic disease. Here we describe an electrocatalytic method for the detection of single-base mismatches as well as DNA base lesions in fully **hybridized** duplexes, based on charge transport through DNA films. Gold electrodes modified with preassembled DNA duplexes are used to monitor the electrocatalytic signal of methylene blue, a redox-active DNA intercalator, coupled to [Fe(CN)6]3-. The presence of mismatched or damaged DNA bases substantially diminishes the electrocatalytic signal. Because this assay is not a measure of differential **hybridization** , all single-base mismatches, including thermodynamically stable GT and GA mismatches, can be detected without stringent **hybridization** conditions. Furthermore, many common DNA lesions and "hot spot" mutations in the human p53 genome can be distinguished from perfect duplexes. Finally, we have demonstrated the application of this technology in a chip-based format. This system provides a sensitive method for probing the integrity of DNA sequences and a completely new approach to single-base mismatch detection.

L12 ANSWER 6 OF 7 MEDLINE on STN DUPLICATE 4
ACCESSION NUMBER: 2001224088 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11172496
TITLE: Bioelectronic detection of point mutations using discrimination of the H63D **polymorphism** of the **Hfe** gene as a model.
AUTHOR: Umek R M; Lin S S; Chen Yp Y; Irvine B; Paulluconi G; Chan V; Chong Y; Cheung L; Vielmetter J; Farkas D H
CORPORATE SOURCE: Clinical Micro Sensors Division of Motorola, Inc, 757 South Raymond Ave., Pasadena, CA 91105, USA.
SOURCE: Molecular diagnosis : a journal devoted to the understanding of human disease through the clinical application of molecular biology, (2000 Dec) 5 (4) 321-8. Journal code: 9614965. ISSN: 1084-8592.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200104
ENTRY DATE: Entered STN: 20010502
Last Updated on STN: 20010502
Entered Medline: 20010426

AB BACKGROUND: A bioelectronic detection platform has recently been developed that facilitates the detection and characterization of nucleic acids. The DNA chip platform is compatible with homogeneous assays because separate labeling and wash steps are not required. A one-step, bioelectronic detection assay was developed to genotype patient samples with respect to the H63D **polymorphism** of the **Hfe** gene, associated with hereditary hemochromatosis. METHODS AND RESULTS: Electrode arrays were modified with DNA capture probes that were perfectly matched to the wild-type or **mutant** allele of H63D. Amplicons containing the **polymorphic** site were **hybridized** with the capture probes on the electrode arrays in the presence of electronically labeled reporter (signaling) probes. Voltammetric analysis of the electrode arrays was conducted first at ambient temperature and then at elevated temperature. The electronic signal was preferentially diminished at elevated temperature from electrodes that **hybridized** with mismatched target amplicons. CONCLUSION: An assay for bioelectronic genotyping of the H63D **polymorphism** was developed and used with six patient specimens to show the feasibility of this system as a model for point **mutation** detection.

L12 ANSWER 7 OF 7 MEDLINE on STN DUPLICATE 5
ACCESSION NUMBER: 2001042583 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10953950
TITLE: A reverse-**hybridization** assay for the rapid and

simultaneous detection of nine **HFE** gene mutations.

AUTHOR: Oberkanins C; Moritz A; de Villiers J N; Kotze M J; Kury F

CORPORATE SOURCE: ViennaLab Labordiagnostika GmbH, Austria..
oberkanins@viennalab.co.at

SOURCE: Genetic testing, (2000) 4 (2) 121-4.
Journal code: 9802546. ISSN: 1090-6576.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200012

ENTRY DATE: Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20001207

AB Hereditary hemochromatosis (HH) is a very common autosomal recessive disorder of iron metabolism and frequently associated with mutations in the **HFE** gene. Molecular genetic testing for **HFE** mutations is considered valuable for carrier identification, as well as for early diagnosis of the disease, allowing simple treatment by phlebotomy and normal survival of patients. We have developed a reverse-**hybridization** assay for the routine diagnosis of eight previously described and one novel (E168Q) **HFE** point mutations. The test is based on multiplex DNA amplification and ready-to-use membrane teststrips, which contain oligonucleotide probes for each wild-type and mutated allele immobilized as an **array** of parallel lines. The procedure is rapid and accessible to automation on commercially available equipment, and by adding new probes the teststrip can easily be adapted to cover an increasing number of mutations.

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FILE 'MEDLINE, BIOTECHDS, EMBASE, BIOSIS, SCISEARCH, CANCERLIT, CAPLUS'
ENTERED AT 11:26:42 ON 03 JUN 2004

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L1          6088 S ROTHBERG B?/AU OR SAWADA R?/AU OR BARTON J?/AU
L2          6857 S HISTOCOMPATIBILITY IRON LOAD### OR HFE
L3          4246 S (POLYMORPHI? OR MUTATION OR MUTANT OR VARIANT) AND (L1 OR L2
L4            41 S L3 AND (EXON 2)
L5            17 DUP REM L4 (24 DUPLICATES REMOVED)
L6             6 S L5 AND (EXON 4)
L7             1 S  (HYBRIDIZ AND (MICROCHIP OR ARRAY))
L8         15485 S  (HYBRIDIZ? AND (MICROCHIP OR ARRAY))
L9             0 S L5 AND L8
L10            0 S L8 AND L4
L11           16 S L8 AND L3
L12            7 DUP REM L11 (9 DUPLICATES REMOVED)
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